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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,988	11/20/2003	Larry C. Mattheakis	CYTOP135XI	1753
22434	7590	01/29/2008	EXAMINER	
BEYER WEAVER LLP P.O. BOX 70250 OAKLAND, CA 94612-0250			SRIVASTAVA, KAILASH C	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/719,988	MATTHEAKIS ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Dr. Kailash C. Srivastava	1657

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

1) Responsive to communication(s) filed on 06 November 2007.

2a) This action is FINAL.                  2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

4) Claim(s) 1-11 and 20-27 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-11 and 20-27 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/ are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 10/15/2007.

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_.

## DETAILED ACTION

1. The amendment and response filed 06 November 2007 to Office Action mailed 11 April 2007 is acknowledged and entered.
2. In regard to the Statement, "Claims 1-11 and 20-27 are pending" and "All pending Claims have been rejected" (see Remarks filed 06 November 2007, Page Numbered as 5, Lines 1 and 3); the record should be corrected because Claims 20-27 are newly filed claims accompanying response filed 06 November 2007. Consequently, "phrase, "all pending Claims have been rejected" is an incorrect statement. Claims 20-27 have been presented for examination for the first time in the instant application.

### Withdrawn Objections and Rejections

3. In view of amendments/ remarks and arguments filed in response cited supra, the following objections/rejections in the Office Action mailed 11 April 2007 are hereby withdrawn:

- Objection to Claims 1, 2, 8-9 and 11;
- Insufficient antecedent basis rejections to Claims 2 and 5 under 35 U.S.C. §112, second paragraph;
- Anticipatory rejection to Claims 1, 7 and 10-11 under 35 U.S.C. §102(b) as anticipated by Aljajeh et al. (Indian Childhood Cirrhosis-Like Liver Disease in an Arab Child. A Brief Report. 1994. Virchows Archiv, Volume 424, Pages 225-227).
- Obviousness rejection to Claims 1-11 under 35 U.S.C. § 103(a) as obvious over combined teachings from Aljajeh et al. (Indian Childhood Cirrhosis-Like Liver Disease in an Arab Child. A Brief Report. 1994. Virchows Archiv, Volume 424, Pages 225-227) in view of Powers et al. (A Microfabricated Array Bioreactor for Perfused 3D Liver Culture. 2002. Biotechnology & Bioengineering, Volume 78, Pages 257-269) and further in view of Le Cluyse et al (Expression and Regulation of Cytochrome P450 Enzymes in Primary Cultures of Human Hepatocytes. Journal of Biochem Molecular Toxicology. 2000. Volume 4, Number 4, Pages 177-188).

## Claims Status

4. Claims 12-19 have currently been cancelled.
5. Claims 20-27 have currently been added.
6. Claims 1 and 11 have currently been amended.
7. Claims 1-11 and 20-27 are currently pending and are examined on merits.

### ***Claim Rejections-35 U.S.C. § 101***

8. The following is a quotation of 35 U.S.C. § 101 that form the basis for the rejections under this section made in this Office action:

*Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.*

9. Claims 1-11 and 20-27 are rejected under 35 U.S.C. § 101 as being drawn to nonstatutory subject matter.

Claims 1-11 and 20-27 are drawn to a computation method, i.e., a process. A statutory process must include a step of a physical transformation, or produce a useful, concrete, and tangible result (*State Street Bank & Trust Co. v. Signature Financial Group Inc.* CAFC 47 USPQ2d 1596 (1998), *AT&T Corp. v. Excel Communications Inc.* (CAFC 50 USPQ2d 1447 (1999))). The instant claims do not result in a physical transformation, thus the Examiner must determine if the instant claims include a useful, concrete, and tangible result.

As noted in *State Street Bank & Trust Co. v. Signature Financial Group Inc.* CAFC 47 USPQ2d 1596 (1998) below, the statutory category of the claimed subject matter is not relevant to a determination of whether the claimed subject matter produces a useful, concrete, and tangible result:

The question of whether a claim encompasses statutory subject matter should not focus on which of the four categories of subject matter a claim is directed to 9-- process, machine, manufacture, or composition of matter--but rather on the essential characteristics of the subject matter, in particular, its practical utility. Section 101 specifies that statutory subject matter must also satisfy the other "conditions and requirements" of Title 35, including novelty, nonobviousness, and adequacy of disclosure and notice. See *In re Warmerdam*, 33 F.3d 1354, 1359, 31 USPQ2d 1754, 1757-58 (Fed. Cir. 1994). For purpose of our analysis, as noted above,

claim 1 is directed to a machine programmed with the Hub and Spoke software and admittedly produces a "useful, concrete, and tangible result." Alappat, 33 F.3d at 1544, 31 USPQ2d at 1557. This renders it statutory subject matter, even if the useful result is expressed in numbers, such as price, profit, percentage, cost, or loss.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful" the claim must produce a result that is specific and substantial. For a claim to be "concrete" the process must have a result that is reproducible. For a claim to be "tangible" the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments.

10. Claims 1-11 and newly presented Claims 20-27 as currently presented do not require production of a tangible result in a form that is useful to the user of the method or the apparatus. A tangible result requires that the claim must set forth a practical application to produce a real-world result.

In regards to "useful, concrete and tangible" result requirement of the statute, each one of Claims 1-11 and 20-27 lack those features because the claims merely describe the steps of what has been done. There is no definition of whether the claimed "computational Method" with the application of claimed "computational device" indeed obtained the required data from images of hepatocytes, or the outcome of quantitative evaluation, or features distinguishing those characteristics of said hepatocytes, or the classification of said hepatocytes into each or any of the categories listed in Claims 1 (b) or in Claim 24(b). Said form of "useful, concrete and tangible" result would be a picture, micrograph, or a chart or a graph outputted in a display (see for e.g., Figure 3 in US Patent 6,876,760 B1).

This rejection could be overcome by amendment of the claims to recite that a result of the process is outputted to a display, or to a user, or in a graphical format, or in a user readable format, or by including a result that is a physical transformation. The applicants are cautioned against introduction of new matter in an amendment to overcome instant rejection.

### ***Claim Rejections - 35 U.S.C. § 103***

11. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

*A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.*

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

13. Claims 1-7, 9-11 and newly presented Claims 20-27 are rejected under 35 U.S.C. § 103 (a) as obvious over combined teachings from Vaisberg et al. (U.S. Patent 6, 876,760 B1) in view of Aljajeh et al. (Indian Childhood Cirrhosis-Like Liver Disease in an Arab Child. A Brief Report. 1994. Virchows Archiv, Volume 424, Pages 225-227) and further in view of each of Powers et al. (A Microfabricated Array Bioreactor for Perfused 3D Liver Culture. 2002. Biotechnology & Bioengineering, Volume 78, Pages 257-269) and f Le Cluyse et al (Expression and Regulation of Cytochrome P450 Enzymes in Primary Cultures of Human Hepatocytes. Journal of Biochem Molecular Toxicology. 2000. Volume 4, Number 4, Pages 177-188).

Claims recite a computational method with the application of a computational device to assess hepatotoxicity of a stimulus via analyzing a hepatocyte image to obtain information on hepatocytes, wherein said information manifests quantitative features to classify ≥1 hepatotoxic pathologies because of the stimulus, said ≥1 pathologies being among: apoptosis, cholestasis, cirrhosis, fibrosis, necrosis or steatosis. In said method, hepatocyte cultures are exposed to varying quantities of said stimulus, said stimulus being a chemical, wherein multiple hepatocytes are located on a plastic or glass support and each culture is exposed to a distinct stimulus. Said images are analyzed on segments and manifested information is on membrane permeability, condensation etc. among a variety of parameters.

Regarding Claims 1-2, 7, 10-11, 20-21, 23-25 and 27, Vaisberg et al. teach computational analysis of imaged hepatocytes in various stages of their development, wherein utilizing a computational device, Vaisberg et al. analyze the nuclei images from a plurality of hepatocyte nuclei, segment said hepatocytes and present results on the computational analysis of images of said hepatocytes (Abstract, Column 15, Line 45 to Column 16, Line 49, Figure 3, Claims 25, 53, 54, 84 and 93 for e.g.,). Vaisberg et al., do not explicitly discuss the computational analysis of the images of pathological hepatocytes, that the hepatocytes were *in vitro*, growing on a single support, wherein each *in vitro* culture is exposed to a distinct, different quantities of stimulus while on a glass or a plastic support, immortalized and co-cultured with support cells to express ≥1 cytochrome P450 enzyme.

Regarding Claims 1-2, 7, 10-11, 20-21, 23-25 and 27; Aljajeh et al. teach methods to computationally quantify through visual examination a chemical stimulus mediated hepatotoxicities, viz. cholestasis, fibrosis and necrosis in photo and micrographs obtained from photo and electron microscopic observation on hepatocytes in liver tissue of a patient. Said assessment, based on observed changes in hepatocyte organelle structure (e.g., cellular membrane and endoplasmic reticulum) demonstrated diagnosis of cholestasis, fibrosis and necrosis in photo and electron micrographs respectively (See, e.g., legend to Figure 2, Lines 3 and 5 and Abstract). Said necrosis and fibrosis (i.e., hepatotoxicities) were manifestations of effect of higher hepatic copper concentration (See, Page 727, Column 1, Lines 12-23). Photo and electron micrographs, inherently are images of the hepatocytes as observed in a photo, or an electron microscope. Note that diagnosis to differentiate between different types of hepatotoxicities and identification that hepatotoxicity exists is in and by itself a computational quantification, wherein the device is the eye and computation is the distinction of different hepatotoxicity. Aljajeh et al. also mention that hepatic copper concentrations were high in said patient. Clearly the abnormal hepatocyte morphology observed was because of said stimulus, which is inherently chemical stimulus. Also, please note that Aljaleh et al. describe  $\geq 1$  hepatotoxic pathologies based  $\geq 1$  hepatocyte features (i.e., membrane and endoplasmic reticulum morphologies). Note that Aljajeh et al., made those observations on liver tissue hepatocytes obtained from a patient. Intrinsically, said hepatocytes were grown in a solid or liquid medium. Hepatocytes in liver are in a solid medium surrounded by liquid and while there, hepatocytes grow. A cell culture by art-known definition is growth of cells in a nutrition medium. Consequently, Aljajeh et al. teach culturing said hepatocytes. Thus, Aljajeh et al's teachings encompass the limitation of exposing the hepatocyte culture to the stimulus. Aljajeh et al., do not explicitly demonstrate that the hepatocytes were in vitro, growing on a single support, wherein each in vitro culture is exposed to a distinct, different quantities of stimulus while on a glass or a plastic support, immortalized and co-cultured with support cells. To express  $\geq 1$  cytochrome P450 enzyme.

Regarding Claims 3-7, 22-23 and 26, Powers et al. teach hepatocyte cultivation in a bioreactor housed with a support and cells are continuously perfused through the 3D tissue mass, the stimulus is perfusion of culture medium. Powers et al. further teach studying the behavior of primary rat hepatocyte culture comprised of hepatocytes and non-parenchymal cells (Abstract, Page 257, Column 2, Lines 49-52), wherein said culturing is in the macro bioreactor made of stainless steel equipped with a glass window and the millireactor made of polycarbonate, the two being separated by plastic scaffolds (Page 259, Column 1, Below Figure 2, Lines 12-20). Also note that the fluid shear of perfusion with the hepatocyte growth medium (HGM) is in range of  $<2$  dyne  $\text{cm}^{-2}$  (Abstract and Page, 260, Column 1, Lines

1-3). Additionally Powers et al. demonstrate repeated *in situ* imaging of tissue structure with two photon microscopy (Abstract, Lines 43-46). Thus, teachings from Powers et al. encompass each of the components in instant claims 2-7, viz:

- i. imaging hepatocytes;
- ii. hepatocytes cultured on support structures;
- iii. *in vitro* culture exposed to distinct stimuli (i.e., intrinsically range of perfusion <2 dyne cm<sup>2</sup>) as the perfusion liquid flows down the culture the stimulus of chemical in dynes per cm<sup>2</sup> will be different through the 3D hepatocyte mass);
- iv. A chemical is the stimulus to which the cells are exposed before imaging (i.e., perfusion with HMG);
- v. hepatocytes co-cultured with support cells (i.e., the culture is primary hepatocyte where in the cells have been obtained from liver and are comprised of non-parenchymal and hepatocytes);
- vi. intrinsically teach imaging of hepatotoxicity of a stimulus because Powers et al. teach that their bioreactor system is an “applicable platform for the studies of *in vivo* physiology and pathology in an *in vitro* environment” (See Page 268, Column 1, Lines 53-56).

Regarding Claim 9, Cluyse et al. teach each and every limitation except for transforming a hepatocyte because they teach cultivation of human hepatocytes and induction of P450 enzymes in human hepatocytes cultivated in “sandwich” cultures in a number of culture media to observe P450 enzyme expression (Abstract, Lines 1-19; Page 178, Column 2, Line 48 to Page 179, Column 1, Line 32).

A person of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the teachings from each one of Aljajeh et al., Powers et al. and Cluyse et al. in to the teachings from Vaisberg et al., because as pointed out Aljajeh et al. teach a method of assessing the hepatotoxicity via analyzing the hepatocyte images to obtain information on chemical stimulus –mediated hepatotoxicity manifested by the alterations in hepatocyte organelle (e.g., cell membrane) structures, while Powers et al. teach imaging hepatocyte cultured in a bioreactor wherein said bioreactor has facilities to cultivate in co-culture hepatocytes and support cells on scaffolds of plastic as a function of a chemical stimulus, wherein said imaging is applicable to assess hepatotoxicity (See, e.g., Page 268, Column 1, Lines 53-56) and Cluyse et al. teach expression of P450 enzymes in cultured hepatocytes in presence of a number of different chemical stimuli (Abstract, Lines 1-19; Page 178, Column 2, Line 48 to Page 179, Column 1, Line 32).

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of each one of Vaisberg et al., Aljajeh et al.,

Powers et al., and Cluyse et al. to obtain a method to computationally assess utilizing a computational device the hepatotoxicity of a chemical stimulus via analyzing images of hepatocytes cultured in presence of a chemical stimulus and observing altered manifestations in hepatocyte organelle, because Aljajeh et al. teach a method of assessing the hepatotoxicity via analyzing the hepatocyte images to obtain information on chemical stimulus-mediated hepatotoxicity manifested by the alterations in hepatocyte organelle (e.g., cell membrane) structures, while Powers et al. teach imaging hepatocyte cultured in a bioreactor wherein said bioreactor has facilities to cultivate in co-culture hepatocytes and support cells on scaffolds of plastic as a function of a chemical stimulus, wherein said imaging is applicable to assess hepatotoxicity and Cluyse et al. teach expression of P450 enzymes in cultured hepatocytes in presence of a number of different chemical stimuli. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman*, 1943 C.D. 518. Applicants invention is predicated on an unexpected result, which typically involves synergism, an unpredictable phenomenon, highly dependent upon specific proportions and/or amounts of particular ingredients. Any mixture of the components embraced by the claims which does not exhibit an unexpected result (e.g., synergism) is therefore ipso facto unpatentable.

Accordingly, the instant claims, in the range of proportions where no unexpected results are observed, would have been obvious to one of ordinary skill having the above-cited references before him.

From the explanations of teachings of the cited references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. Claims 8-9 are rejected under 35 U.S.C. § 103 (a) as obvious over combined teachings from Vaisberg et al (US Patent 6, 876, 760 B1) in view of Aljajeh et al. (*Indian Childhood Cirrhosis-Like Liver Disease in an Arab Child. A Brief Report*. 1994. *Virchows Archiv*, Volume 424, Pages 225-227); Powers et al. (*A Microfabricated Array Bioreactor for Perfused 3D Liver Culture*. 2002. *Biotechnology & Bioengineering*, Volume 78, Pages 257-269) and Le Cluyse et al (*Expression and Regulation of Cytochrome P450 Enzymes in Primary Cultures of Human Hepatocytes*. *Journal of Biochem Molecular Toxicology*. 2000. Volume 4, Number 4, Pages 177-188) and further in view of Morel et al (1990,

Expression of Cytochrome P-450 Enzymes in Cultured Human Hepatocytes, Eur. J. Biochem., Volume 191, Pages 437-333).

Claims 8-9 additionally recite, said hepatocytes are transformed and further modified to express  $\geq 1$  cytochrome P450 enzyme.

Teachings from Vaisberg et al., Aljajeh et al., Powers et al. and Cluyse et al. have been discussed supra. The elements in Claims 8-9, especially in regard to transformed hepatocytes is not explicitly clear from those teachings. Morel et al. teach methods to transform cultured human primary culture hepatocytes to produce specific cytochrome P-450 IIIA and P-450 IIC8/9/10. The expression for individual P-450 products was induced via transforming human hepatocytes through cultivation in standard medium supplemented with each of rifampicin, 3-methylcholanthrene or Phenobarbital in separate flasks. Subsequently, with each medium change, the basic cell culture medium was consistently supplemented with the same inducing agent and the transformed hepatocytes were harvested after the third addition of inducers (Page 438, Column 1, Lines 44-65 and cytochrome P-450 expression was assayed (Page 439, Column 1, Line 10 to Page 439, Column 2, Line 32).

A person of ordinary skill in the art at the time the invention was made would have been motivated to incorporate the teachings from Morel et al, in to the combined teachings from each one of Powers et al., Cluyse et al. and Aljajeh et al., because as pointed out above, Aljajeh et al. teach a method of assessing the hepatotoxicity via analyzing the hepatocyte images to obtain information on chemical stimulus –mediated hepatotoxicity manifested by the alterations in hepatocyte organelle (e.g., cell membrane) structures, while Powers et al. teach imaging hepatocyte cultured in a bioreactor wherein said bioreactor has facilities to cultivate in co-culture hepatocytes and support cells on scaffolds of plastic as a function of a chemical stimulus, wherein said imaging is applicable to assess hepatotoxicity (See, e.g., Page 268, Column 1, Lines 53-56), Cluyse et al. teach expression of P450 enzymes in cultured hepatocytes in presence of a number of different chemical stimuli and Morel et al teach transformation of human hepatocytes in culture to express different cytochrome P-450 products depending upon the inducer for transformation.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the teachings of each one of Aljajeh et al., Powers et al., Cluyse et al. and Morel et al. to obtain a method to assess the hepatotoxicity of a chemical stimulus via analyzing images of hepatocytes cultured in presence of a chemical stimulus and observing altered manifestations in

hepatocyte organelle, because Aljajeh et al. teach a method of assessing the hepatotoxicity via analyzing the hepatocyte images to obtain information on chemical stimulus –mediated hepatotoxicity manifested by the alterations in hepatocyte organelle (e.g., cell membrane) structures, while Powers et al. teach imaging hepatocyte cultured in a bioreactor wherein said bioreactor has facilities to cultivate in co-culture hepatocytes and support cells on scaffolds of plastic as a function of a chemical stimulus, wherein said imaging is applicable to assess hepatotoxicity, Cluyse et al. teach expression of P450 enzymes in cultured hepatocytes in presence of a number of different chemical stimuli and Morel et al. teach transformation of human hepatocytes by a variety of inducers to illicit expression of a different P-450 product. This rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, *In re Sussman*, 1943 C.D. 518. Applicants invention is predicated on an unexpected result, which typically involves synergism, an unpredictable phenomenon, highly dependent upon specific proportions and/or amounts of particular ingredients. Any mixture of the components embraced by the claims which does not exhibit an unexpected result (e.g., synergism) is therefore ipso facto unpatentable.

Accordingly, the instant claims, in the range of proportions where no unexpected results are observed, would have been obvious to one of ordinary skill having the above-cited references before him.

From the explanations of teachings of the cited references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### Conclusion

15. For reasons aforementioned, no Claims are allowed.
16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). Alternatively, status inquiries should be directed to the receptionist whose telephone number is (703) 308-0196.

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18 January 2008

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